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381892,695
APPLICATION NUMBER 087892,695 FILING DATE 07/15/97 FIRST NAMED APPLICANT GRAY ATTY. DOCKET NO. J 023070068930

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EXAMINER

UNGAR, S
ART UNIT PAPER NUMBER

1642/642 13

DATE MAILED 02/01/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- ☒ Responsive to communication(s) filed on 12/23/98
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 30 days, or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-47 is/are pending in the application.
Of the above, claim(s) is/are withdrawn from consideration.
- ☐ Claim(s) is/are allowed.
- ☐ Claim(s) is/are rejected.
- ☐ Claim(s) is/are objected to.
- ☒ Claim(s) 1-47 are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number)
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received:

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s).
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

1. Applicant's specification, as filed, presents two claims that are both numbered as claim 1, followed by claims 2-46. These claims have been renumbered, under Rule 126, as claims 1-47, respectively.
2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.
3. Applicant's election with traverse of Group II, SEQ ID NO:9 and SEQ ID NO:10, in Paper No. 15, filed 6/01/99 is acknowledged.

The traversal is on the ground(s) that the examiner has failed to provide sufficient reasoning or evidence to show that the present claim 26 constitutes an improper Markush group. Thus, at most, an election of species is required. Further, the traversal is on the ground(s) that under the directions of MPEP 803.04, the requirement to elect a single sequence is improper, as at least 10 of the 12 sequences must be examined. These arguments have been carefully considered and are not found persuasive.

As stated in the restriction requirement mailed on 2/1/99, method claim 26 has presented in improper Markush format (see **Ex parte Markush**, 1925 C.D. 126 and **In re Weber**, 198 USPQ 334). The method of claim 26 improperly joins SEQ ID NO:1-13, polynucleotide sequences that differ in structure and function to such an extent that they are considered separately patentable. As noted on pages 22-23 of the specification, each of SEQ ID NO:1-9 and 12-13 are related to "unique genes." For example: SEQ ID NO:1 (3,000 bp) is a "3kb transcript with sequence identity to a tyrosine kinase gene;" SEQ ID NO:3 represents a "6-7 kb transcript which shows homology to C2H2 zinc finger genes;" SEQ ID NO:6 (2821 bp) "encodes a quanine cyclase activating protein which is involved in the biosynthesis of cyclic AMP;" SEQ ID NO:9 (10365 bp) and SEQ ID NO:10 (3186 bp) represent "the entire nucleotide sequence" of the ZABC-1 protein, a zinc finger protein amplified in breast cancer; and SEQ ID NO:13 "provides sequence from a genomic clone which is similar to known rat and mouse cyclophilin cDNAs," accordingly, "SEQ ID NO:13 is a putative human cyclophilin gene." Thus, as summarized above,

data presented on pages 22-23 of the specification documents the differing structural and functional characteristics of each of each of SEQ ID NO:1-9, 11 and 13. Each of these SEQ ID NO: is a lengthy polynucleotide sequence, encoding a polypeptide that is biologically and chemically distinct, unrelated in structure and function. Thus, restriction for examination purposes as indicated is proper.

Further, the applicant argues that under the guidelines set forth in MPEP 803.04, they are due the examination of ten different SEQ ID NO:, that restriction to a single polynucleotide sequence is improper. This is not found persuasive. As stated in MPEP 803.04, "Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141."

Clearly different searches and issues are involved in the examination of each of Group I-VI and each various SEQ ID NO:. For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 1-47 are pending.

Claims 1-25, 29-36, 39-40, 42-47, drawn to non-elected inventions, are withdrawn from examination.

Claims 26-28, 37-38 and 41 are examined on the merits. Claims 26-28 and 41 are examined to the extent that they read on SEQ ID NO:9 and SEQ ID NO:10.

5. Claims 26-28, 37-38 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is vague and indefinite in the recitation of non-elected SEQ ID NO:s.

Claim 26 is vague and indefinite in the recitation "hybridizes selectively." It is unclear what type of "hybridization" (base pairing of DNA) qualifies as "selective."

Claim 41 is vague and indefinite in the recitation "is used." It is unclear how the intended use modifies the claimed method itself. The claimed method lacks actual method steps directed at accomplishing this intended use.

6. Claims 26-28, 37-38 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement commensurate with the scope of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 26 is drawn to a "method of screening for neoplastic cells in a sample," the method comprising contacting a nucleic acid sample with a probe which hybridizes selectively to a target polynucleotide sequence comprising a sequence selected from either SEQ ID NO:9 or SEQ ID NO:10; and detecting the formation of a hybridization complex. Thus, the mere hybridization of a probe to nucleic acids in the sample, where the probe is capable of hybridizing to a portion of either SEQ ID NO:9 or SEQ ID NO:10, is to be indicative of the presence of neoplastic cells in the sample. SEQ ID NO:10 is the cDNA sequence of the ZABC-1 protein (having the amino acid sequence of SEQ ID NO:11) a zinc finger protein amplified in breast cancer, and SEQ ID NO:9 is a portion of the genomic sequence of the ZABC-1 gene. The ZABC-1 gene maps to the 20q13.2 amplicon, a genomic region that is amplified in various cancers (see p. 23 of the specification). While it is noted that this newly cloned gene, is "amplified" and "over expressed" in a variety of different cancer cells, it has to be assumed that an unamplified copy of this gene is to be found in all human genomes, and that a cDNA transcript may be synthesized in some non-cancerous cells. This assumption is supported by Collins et al (PNAS 95:8703, 1998). Collins discloses the ZNF217 protein, a protein that has the same amino acid sequence (Fig 3b) as SEQ ID NO:11, and states that a major 6-kb ZNF217 transcript is detected "in most tissues except adult brain and fetal kidney" and an additional 4-kb transcript is present in testis (see p.8706, col.

2). Additionally, various YAC, P1 and BAC genomic clones, derived from non-cancerous sources, hybridize to probes derived from the nucleotide sequences encoding the ZNF217 protein. Thus, sample derived from non-neoplastic tissue sources would be expected to hybridize to probes prepared from SEQ ID NO:9 or SEQ ID NO:10. Thus, the formation of a hybridization complex in a sample with a probe that detects either of SEQ ID NO:9 or SEQ ID NO:10 can not be interpreted to be indicative of the presence of neoplastic cells in the sample. It would require additional experimentation of one of skill in the art to determine if a positive signal was indicative of neoplastic cells.

Claim 41 is drawn to "the method of claim 26, wherein the probe is used to identify the presence of a mutation in the target polynucleotide sequence." In claim 26, a sample is contacted with a "probe" which hybridizes selectively to a target sequence comprising either SEQ ID NO:9 or SEQ ID NO:10 and a stable hybridization complex is formed. Absent additional experimentation and additional method steps, one of skill in the art can not make a determination as to the presence of a mutation in the target sequence merely by the formation of a hybridization complex with the broad collection of probes encompassed by claim 26.

7. Polynucleotide sequences identical to SEQ ID NO:9 and 10 are found in parent applications 08/785,532 (filed 1/17/97) and 08/731,499 (filed 10/16/96). Polynucleotide sequences identical to SEQ ID NO:9 and 10 are not found in parent application 08/860,395 (filed 7/15/96). Therefore for the application of the art, priority is granted to the filing date of parent 08/731,499 application, filed 10/16/96.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 26-28, 37-38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO9401548 in view of Accession Number Q63862 (29-Jan-1995). WO9401548 teaches method of detecting comprising contacting a nucleic acid sample with a probe derived from a fragment of polynucleotide sequence and forming a detectable hybridization complex (see p. 7, lines 21-37, p.10, lines 28-37 and p.12, lines 17-25). WO9401548 does not teach the use of probes that would hybridize to either of SEQ ID NO:9 or SEQ ID NO:10. However, Accession Number Q63862 teaches such probes. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the polynucleotide of Accession Number Q63862 as a probe in the detection method of WO9401548. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of WO9401548, on the general usefulness of such hybridization based detection method for genetic analysis, identifying manipulable targets related to disease and for obtaining extended cDNA clones.

10. Claims 26-28, 37-38 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO9401548 in view of either of Accession Numbers W05407 (23 April 1996) or N70546 (14 March 1996). WO9401548 teaches method of detecting comprising contacting a nucleic acid sample with a probe derived from a fragment of polynucleotide sequence and forming a detectable hybridization complex (see p. 7, lines 21-37, p.10, lines 28-37 and p.12, lines 17-25). WO9401548 does not teach the use of probes that would hybridize to either of SEQ ID NO:9 or

SEQ ID NO:10. However, Accession Numbers W05407 and N70546 Q63862 teach such probes. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the polynucleotide sequences of either of Accession Numbers W05407 or N70546 as a probes in the detection method of WO9401548. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of WO9401548, on the general usefulness of such hybridization based detection method for genetic analysis, identifying manipulable targets related to disease and for obtaining extended cDNA clones.

11. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

12. Claims 36-37 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 35-36 of copending Application No. 08/731,499. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

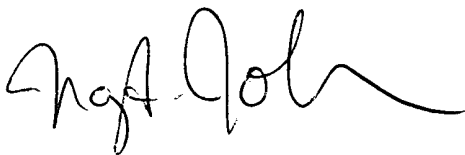
A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 26-28, 36-37 and 41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24-26, 35-36 and 38 of copending Application No. 08/731,499. Although the conflicting claims are not identical, they are not patentably distinct from each other because all claims are drawn to methods of screening for neoplastic cells comprising contacting a sample with a nucleic a probe that hybridizes to SEQ ID NO:9 or SEQ ID NO:10. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 26-28, 36-37 and 41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-28, 37-38, 56-57 and 61-63 of copending Application No. 08/785,532. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims are drawn to methods of screening for neoplastic cells comprising contacting a sample with a nucleic a probe that hybridizes to SEQ ID NO:9 or SEQ ID NO:10. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Johnson whose telephone number is (703) 305-5860. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



NANCY A. JOHNSON, PH.D
PRIMARY EXAMINER

February 6, 2000